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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,277	04/23/2001	Ulrich Feige	A-688A	3317

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EXAMINER
WESSENDORF, TERESA D

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/840,277	Applicant(s) FEIGE ET AL.	
	Examiner T. D. Wessendorf	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-5,7-13 and 25* is/are pending in the application.

4a) Of the above claim(s) *10-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5,7-9,13 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claims 2-13 and 25, the species of Seq. ID. 136 and Seq. ID. 2 in Paper No. 11 are acknowledged. The traversal is on the ground(s) that amended claim 25 becomes a subset of claim 2. Claim 3 is directed toward a subset of the compounds encompassed by claim 2. Claims 4 and 5 use substituents encompassed by claim 2. A search of claim 2 would necessarily overlap a search of claims 3-5 and 25. It is further argued that this will not impose undue burden on the examiner. In view of the amendments to the claims, the restriction requirement is revised. Claims 3-5 and 25 will be examined with the elected group II. [It is noted that there is no Seq. ID. 136, as elected. The Sequence Listing contains only 135 sequences. The Preliminary Amendment changed Seq. ID. 136 to Seq. ID. 95. Seq. ID. 95 will therefore be treated as the elected species].

The requirement is still deemed proper and is therefore made FINAL.

Claims 10-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species and invention, there being no allowable generic or

linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

Status of Claims

Claims 1, 6 and 14-24 have been cancelled in the response of 1/30/03.

Claims 10-12 are withdrawn from consideration, as stated supra.

Claims 2-5, 7-9, 13 and 25 are under examination.

Specification

The incorporation of essential material in the specification (page 17, lines 30-31) by reference to a World Patents WO 95/14714 and 97/08203 is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors

(grammatical, typographical and idiomatic). Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-5, 7-9, 13 and 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to provide a written description for any kind of integrin/adhesion antagonist peptides having the amino acid sequence of ID. 95 fused to an Fc domain of IgG. Except for Seq ID. 95-Fc fusion, there is no other related peptide described in the specification that has been fused to Fc. The fact is, the specific embodiments in the specification, Example 3, page 57 states that peptide, YIGSR, when fused to Fc was proteolyzed. All the degradation occurred after the arginine

residue (at the junction between the YIGSR repeats). In order to eliminate said degradation, peptide Seq. ID.95 (and 96) was designed by applicants. The peptide(s) result in the desired inhibitory function. Accordingly, the specification does not provide sufficient guidance to direct a skilled artisan to the other peptide sequences containing YIGSR fragments. That is, peptides that is ineffectual because of degradation. Rather, than those peptides with the desired optimized function or at least a retained function.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-5, 7-9, 13 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 2 is indefinite as to the use of "/" sign. It is suggested that applicants recite for a prepositional phrase for said sign.

B. Claim 13 is indefinite in referring to Tables 2-6. It is suggested that applicants simply recites the Seq. ID. Nos.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-5, 7-9, 13 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitty et al (US 2002/0155547) in view of Mu (BBRC, Ref. DB).

Witty discloses at page 3, lines 1-27 an isolated polypeptide having the amino acid sequence X--Y--Z, wherein X is a polypeptide having the amino acid sequence, or portion thereof, consisting of the amino acid sequence of interferon beta; Y is an optional linker moiety; and Z is a polypeptide comprising at least a portion of a polypeptide other than interferon beta. Optional moiety Y and required moiety Z may be linked to either the N- or C-terminus of interferon beta (X). Preferably, X is human interferon-beta-1a. Z is at least a portion of a constant region of an immunoglobulin and can be derived from an immunoglobulin of the IgG class such as IgG1, IgG2, IgG3 and IgG4. The constant region of human IgG, contains

3 constant regions (CH1, (hinge), CH2 and CH3. In the fusion proteins, the constant region contains at least the hinge, CH2 and CH3 domains. Also, see Fig. 3, page 5. Whitty further discloses at paragraph bridging pages 19 and 20, that in the fusion proteins, the interferon-beta-1a polypeptide is fused via its C-terminus to at least a portion of the Fc region of an immunoglobulin. The interferon-beta-1a forms the amino-terminal portion, and the Fc region forms the carboxy terminal portion. In these fusion proteins, the Fc region is preferably limited to the constant domain hinge region and the CH2 and CH3 domains. The Fc region in these fusions can also be limited to a portion of the hinge region, the portion being capable of forming intermolecular disulfide bridges, and the CH2 and CH3 domains. These constant regions may be derived from any mammalian source (preferably human) and may be derived from IgG1, IgG2, IgG3 and IgG4. Whitty describes at page 20, line 24 up to page 21, line 15, a dimeric fusion molecules as well as monomeric or multimeric molecules comprising fusion proteins. Such multimers may be generated by using those Fc regions, or portions thereof, of Ig molecules which are usually multivalent such as IgM pentamers or IgA dimers. Multimers of interferon-beta-1a fusion proteins may be formed using a protein with an affinity for the Fc region of Ig molecules. The polyvalent forms are useful since

they possess multiple interferon beta receptor binding sites. For example, a bivalent soluble interferon-beta-1a may consist of two tandem repeats of amino acids 1 to 166 of SEQ ID NO: 2 (moiety X in the generic formula) separated by a linker region (moiety Y), the repeats bound to at least a portion of an immunoglobulin constant domain (moiety Z).

Alternate polyvalent forms may also be constructed, for example, by chemically coupling interferon-beta-1a/Ig fusions to any clinically acceptable carrier molecule like polyethylene glycol using conventional coupling techniques.

Whitty fails to disclose a fusion protein with laminin of the sequence YIGSR. However, Mu discloses that laminin peptide with YIGSR bioconjugated with polystyrene co-maleic acid results in increase of antimetastic effect. See page 75, col. 1 and 2. Mu further discloses that to be therapeutically useful YIGSR peptide requires in vivo stability that allows administration of YIGSR. Mu discloses similar bioconjugation of other extracellular matrix domains, besides YIGSR, such as Interferons. It would have been obvious to one having ordinary skill in the art at the time the invention was made to replace the interferon in the fusion protein of Whitty with a YIGSR-containing laminin. Mu teaches that Laminin and interferon belong to the family of extracellular matrix domains (active in

adhesion). It would be within the ordinary skill in the art to pick or choose the specific compounds from the family of extracellular matrix domain compounds. Fusion of these peptides to Fc or other compounds such as PEG results in increased in vivo stability. Such in vivo stability would motivate one having ordinary skill in the art. In vivo stability is an important aspect for therapeutic effect of a compound agent in the treatment of any disease particularly, tumors.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A. Schachner et al suggests fusion of Fc and laminin.

Allowable Subject Matter

The elected species is free of prior art. A claim drawn to the fusion of the elected species consisting essentially of Seq. ID. 95 (or 96) fused either at the N or C terminus of Seq. ID. 2 (Fc) would be allowable if made into an independent claim.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
February 21, 2003